CASE REPORT

Neurofibroma of the ulnar nerve in the carpal canal in a dog: treatment by marginal neurectomy

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Peripheral nerve sheath tumours arising in the plexus or peripheral nerves can be treated by limb amputation. There are few reports of these tumours affecting peripheral nerves in the distal regions of the limbs. Here we describe a case of neurofibroma affecting the palmar branch of the ulnar nerve in an Irish setter. Surgical treatment in the region of the carpus by ulnar neurectomy resulted in resolution of chronic thoracic limb lameness. At 11 months following the surgery, clinical examination and MRI did not detect any evidence of recurrence. Neurectomy may be a feasible option for management of selected cases of distally located peripheral nerve sheath tumours.

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INTRODUCTION

Peripheral nerve sheath tumours arise from peripheral or cranial nerves or nerve roots, and often develop from Schwann cells and fibroblasts of the perineurium (Targett *et al.* 1993). They are classified on the basis of their proximity to the remainder of the nervous system as belonging to the root group (involving nerves adjacent to the brain, brainstem or spinal cord), the plexus group (involving the brachial or lumbosacral plexus) and the peripheral group (distal to the brachial or lumbosacral plexus) (Brehm *et al.* 1995, Caplan 2013).

Most peripheral nerve sheath tumours diagnosed in small animals are classified as belonging to the plexus or root group (Caplan 2013) and so neurectomy as the sole treatment is seldom possible because of their involvement of the intervertebral foramen and nerve roots (Caplan 2013).

In contrast, this case report describes results after excision of a peripheral nerve sheath tumour involving the ulnar nerve and reviews the current literature on peripheral nerve sheath tumours in the dog.

CASE HISTORY

A 9-year-old spayed female Irish setter was presented to the hospital with the complaint of a 15-month history of worsening left thoracic limb lameness. The lameness was initially managed with orally administered meloxicam, then a short course of tramadol and paracetamol, which mildly improved the lameness.

On physical examination, the patient had intermittent non-weight-bearing lameness in the left thoracic limb and consistently showed signs of pain during flexion of the left carpus. Conscious proprioception and withdrawal reflexes were difficult to assess due to hyperaesthesia of the affected limb but there was no sign of ataxia or paresis.

Plain helical CT [16-slice Philips Brilliance helical CT (slice thickness 1 mm, kvP 90, mAs 131 using soft tissue and bone filters)] of the left carpus was performed with the dog under general anaesthesia. There were no abnormalities or appreciable soft tissue swelling. MRI of the left antebrachium was performed using a 3 Tesla unit with a surface coil (eight-channel wrist array, Model Discovery MR750; GE Healthcare). There was a round, well-demarcated soft tissue structure with mild homogenous increase in contrast enhancement on the T2- and proton density-weighted sequences that was identified originating deep to the flexor carpi ulnaris muscle and coursing lateral and deep to the deep digital flexor tendon before terminating in the mid third of the metacarpus (Fig. 1A and B). The location of the contrast-enhancing structure coincided with the location of the palmar branch of the ulnar nerve.

Seven weeks following MRI, the patient was anaesthetised for surgery and a palmar approach was made to the left antebrachium. The course of the ulnar nerve was traced from its path distal to the medial epicondyle of the humerus along the palmar

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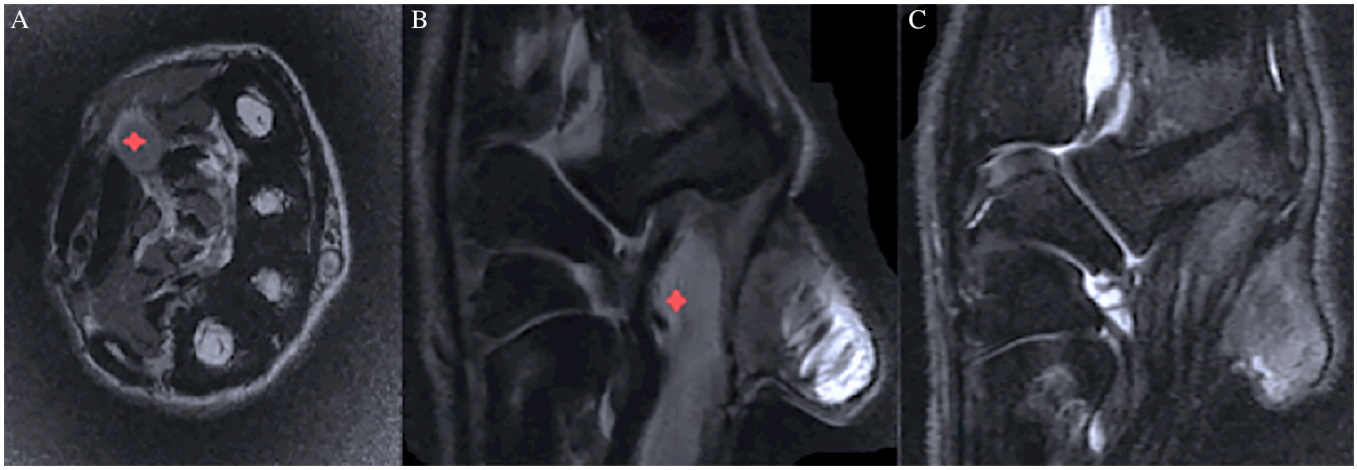

FIG 1. MRI images using proton density-weighted sequence after contrast administration. The tumour is labelled with a red asterisk in images A and B. Image A is in transverse plane sectioned at the level of the proximal metacarpals and images B and C are sagittal sections at the level of the carpus. Image C is from an MRI obtained 11 months following the initial surgery showing absence of a contrast-enhancing structure. In Image A, dorsal is to the right of the image and the top of the image corresponds to the lateral aspect of the antebrachium. In images B and C, dorsal is to the left of the image, palmar to the right, proximal to the top and distal to the bottom

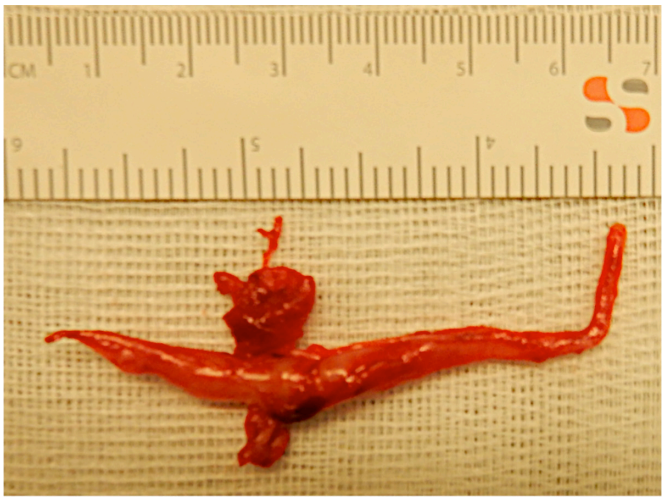

FIG 2. Image of the excised ulnar nerve. The distal part of the nerve is to the left of the image

surface of the antebrachium. Segmental thickening of the ulnar nerve was identified extending from the distal third of the antebrachium, deep to the carpal canal. The ulnar nerve was excised with 2 cm of grossly normal tissue proximal to the lesion at the mid antebrachium, and transected distally at the level of the mid metacarpus without gross margins due to close proximity of the insertion of the digital flexor tendons. The excised nerve was fixed in 10% buffered formalin (Fig. 2).

Histopathologic evaluation of the enlarged nerve showed complete replacement of the normal nerve tissue by an intraneural proliferation of loosely arranged spindeloid cells with thin wavy nuclei, small nucleoli and fine chromatin, interspersed with collagenous stroma (Fig. 3). There was no nuclear pleomorphism or mitotic activity in the spindeloid cells. Luxol Fast Blue stain revealed variable numbers of small myelinated axons interspersed throughout the collagenous tissue. The lesion was initially diagnosed as a benign fibromatous proliferative lesion. Immunoperoxidase staining with S100 revealed small numbers of positive staining Schwann cells in the neoplastic areas. A revised diagnosis of benign peripheral nerve sheath tumour, consistent with a localised intraneural neurofibroma, was made.

The dog was mildly lame following surgery. Serial follow up examinations were performed without tumour staging because the mass was benign. At the 3-month clinical examination the thoracic limb lameness had resolved. Re-examinations at 6 and 11 months following surgery did not reveal signs of neural abnormalities such as motor or sensory deficits. There was no muscle atrophy detectable at 11 months. Cutaneous sensation was apparently normal and there was normal carpal flexion when withdrawal reflexes were tested.

MRI of the left carpus using the same initial scanning protocol was repeated 11 months following surgery. There was no evidence of local tumour recurrence, and the previously identified mass was no longer visible (see Fig. 1C). There was a reduction in muscle mass with patchy areas of increased signal intensity in the T1-weighted images palmar to the metacarpals, consistent with atrophy of the interosseous, adductor digiti quinti and adductor digiti secondi muscles.

DISCUSSION

The most common presenting complaints for dogs with peripheral nerve sheath tumours are unilateral thoracic limb lameness and muscle atrophy, as was seen in our case (Brehm *et al.* 1995). In cases involving the vertebral canal (root group), more severe neurological signs such as absence of cutaneous trunci reflex and Horner's syndrome may be detected (Wheeler et al. 1986). Further diagnostics such as CT, MRI, ultrasound and electrophysiology have been used to identify lesions suspected to be peripheral nerve sheath tumours (Kraft *et al.* 2007, Guilherme & Benigni 2008, Le Chevoir *et al.* 2012). Ultrasound has been suggested as a screening tool because the nerves are seen as hypo-echoic

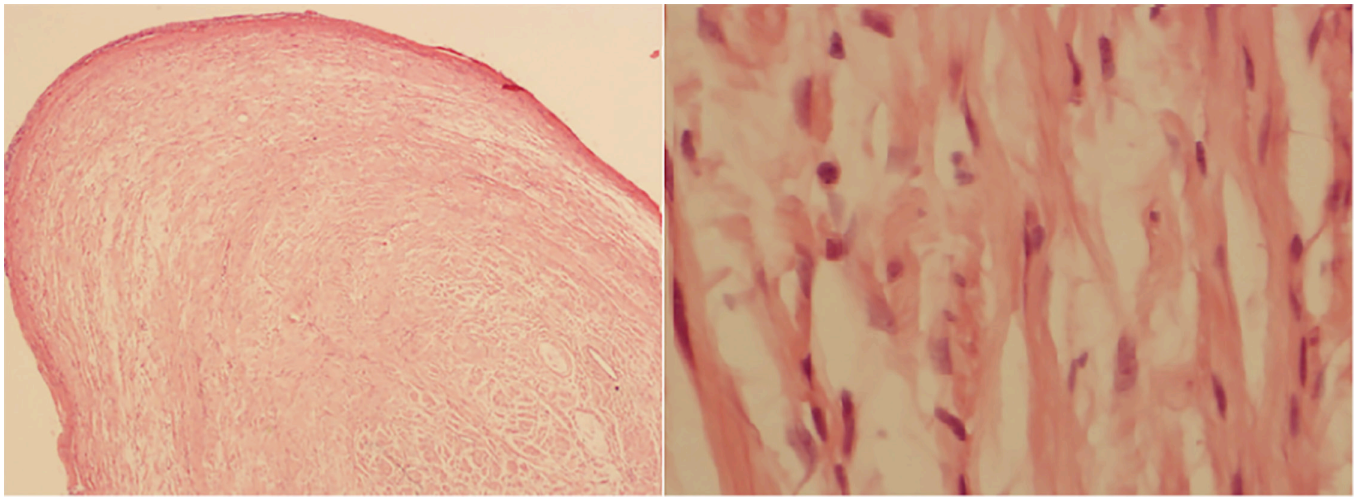

FIG 3. Photomicrograph of the tumour nodule: left-sided image – low-power; right-sided image – high power (H&E)

tubular structures that displace vessels, although they can also be confused with axillary lymph nodes (Rose *et al*. 2005, Guilherme & Benigni 2008).

CT has been used to diagnose brachial plexus masses but relies upon finding contrast rim enhancement around the masses and the smallest dimension of masses detectable in single slices has been previously reported as 1 cm (Rudich *et al*. 2004). MRI is generally more helpful because the majority of peripheral nerve sheath tumours are consistently hyperintense relative to muscle on T2-weighted images and isointense on T1-weighted images (Kraft *et al*. 2007, Guilherme & Benigni 2008). Contrast enhancement may be the only feature in masses in which there is subtle diffuse nerve sheath involvement (Kraft *et al*. 2007). There are currently no MRI characteristics that allow differentiation of inflammatory from neoplastic lesions, or benign from malignant peripheral nerve sheath tumours.

Peripheral nerve sheath tumours in the dog are categorised on whether they originate exclusively from cells with Schwann cell characteristics (schwannoma and perineurioma) or from mixtures of Schwann cells and endoneurial, epineurial or stromal fibroblasts (neurofibromas and malignant peripheral nerve sheath tumours) (Meuten 2002). The cytologic features of the neoplastic cells, cellularity of the tumour, specific histologic patterns, the interstitial matrix material, mitotic rate and evidence of invasive behaviour are evaluated on histopathology. Immunohistochemistry to determine the proportion of Schwann cells and to detect intra-tumoural axons, as well as electron microscopy, are also used to confirm the tumour type (Rodriguez *et al*. 2012).

The three benign peripheral nerve sheath tumours in the dog are schwannoma, neurofibroma and perineurioma (Meuten 2002). Malignant peripheral nerve sheath tumour is the only recognised malignant form. Schwannomas have a densely packed pattern with distinctive histologic features (Antoni types A and B, Verocay bodies). They show diffuse positive immunostaining with Schwann cell markers such as S100, and nerve fibres are absent (Feany *et al*. 1998, Meuten 2002). Perineurioma is a rare tumour that has a specific histologic pattern of neoplastic perineurioma cells around myelinated axonal cores (Higgins *et al*. 2006). Neurofibromas can be intraneural or extraneural and contain a variable mixture of cell types including Schwann cells, epineurial cells and fibroblasts (Feany *et al*. 1998, Fattahian *et al*. 2012). Subclassification of veterinary neurofibromas has been reported and shows good correlation with the classification scheme used in human pathology (Schoniger & Summers 2009).

The histologic characteristics of the neural tumour in this dog together with a low proportion of positive Schwann cells on S100 staining and the presence of small axons within the mass support the diagnosis of intraneural neurofibroma. It can be difficult to distinguish between reactive processes involving nerve tissue and benign tumours in which the cells show little pleomorphism and are mixed with fibrous tissue. There are also subtypes of neurofibroma and schwannoma in which the cellularity can be variable and specific categorisation may not be possible, for example in hybrid benign nerve sheath tumours (Rodriguez *et al*. 2012).

The principles of treatment of peripheral nerve sheath tumours in dogs include excision of the tumour (and nerve), limb amputation and laminectomy when nerve roots are affected (Bradley *et al*. 1982). Much of the current knowledge regarding management of peripheral nerve sheath tumours is extrapolated from treatment of soft tissue sarcomas, with the recommendation being to perform a wide local resection with 2 to 3 cm margins (Dernell *et al*. 1998). Resection of soft tissue sarcomas with complete margins resulted in a median survival time of 1416 days (Dernell *et al*. 1998). In dogs that have tumours affecting the brachial plexus, the reported median survival time is 12 months with amputation alone, and only 5 months in cases affecting the intervertebral foramen (Brehm *et al*. 1995). There is one case report in which epineurotomy was reported for a canine malignant peripheral nerve sheath tumour affecting the radial nerve but this only provided relief from clinical signs for 4 months (Gibson *et al*. 2016). The ulnar nerve divides into caudal cutaneous antebrachial (palmar) and dorsal branches (Bailey & Kitchell 1987).

The palmar branch innervates the caudolateral aspect of the antebrachium, while the test site for the dorsal branch is the lateral surface of the fifth digit (Bailey & Kitchell 1987). The ulnar nerve from the level of the medial epicondyle of the humerus is responsible for motor innervation of the flexor carpi ulnaris and deep digital flexor muscles (Evans & DeLahunta 2010). Signs of sensory or motor deficits were not detected in our case, although there was atrophy of the muscles palmar to the metacarpus on the follow-up MRI that was not apparent during physical examination. Ulnar nerve injury is reported to cause hyperextension of the carpus when weight-bearing on the limb (Hoerlein 1978). We suspect that there were no detectable abnormalities on follow-up examination because the radial nerve (innervates extensors of the thoracic limb) was intact (Hoerlein 1978).

Peripheral nerve sheath tumours affecting the distal limb are rare, and due to the higher incidence of more proximal tumours most authors advocate amputation to ensure complete surgical margins (Targett *et al*. 1993). There are few indications for neurectomy and the functional outcome depends on the structures that the nerve innervates. In this particular case, we were able to demonstrate that the ulnar nerve can be resected without significantly affecting limb function.

The findings in this case suggest that ulnar neurectomy could be an alternative to thoracic limb amputation in selected cases of benign peripheral nerve sheath tumours. Limb function was unaffected by removal of the palmar branch of the ulnar nerve, and relevant neuroanatomy should be considered in cases of distally located peripheral nerve sheath tumours that may be amenable to tumour excision.

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Conflict of interest

No conflicts of interest have been declared.

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